# Clinical trial results:
# A Phase 3 Randomized, Double-blind, Placebo-controlled, Parallel group Efficacy and Safety Study of SHP647 as Induction Therapy in Subjects with Moderate to Severe Ulcerative Colitis (FIGARO UC 302)

## Summary

| | |
|---|---|
| EudraCT number | 2017-000572-28 |
| Trial protocol | IE HU SK BG GR BE ES PT FR |
| Global end of trial date | 06 October 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 12 April 2021 |
| First version publication date | 12 April 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | SHP647-302 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03259308 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Shire |
| Sponsor organisation address | 300 ShireWay, Lexington, United States, MA 02421 |
| Public contact | Study Director, Shire, ClinicalTransparency@takeda.com |
| Scientific contact | Study Director, Shire, ClinicalTransparency@takeda.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 06 October 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 October 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of ontamalimab in inducing remission, based on composite score of subject reported symptoms and centrally read endoscopy, in subjects with moderate to severe Ulcerative Colitis (UC).

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996), the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 December 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 1 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 2 |
| Country: Number of subjects enrolled | Bulgaria: 24 |
| Country: Number of subjects enrolled | Canada: 4 |
| Country: Number of subjects enrolled | Colombia: 6 |
| Country: Number of subjects enrolled | Estonia: 1 |
| Country: Number of subjects enrolled | Greece: 1 |
| Country: Number of subjects enrolled | Hungary: 28 |
| Country: Number of subjects enrolled | Ireland: 1 |
| Country: Number of subjects enrolled | Japan: 16 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Lebanon: 1 |
| Country: Number of subjects enrolled | Mexico: 14 |
| Country: Number of subjects enrolled | New Zealand: 3 |
| Country: Number of subjects enrolled | Portugal: 8 |
| Country: Number of subjects enrolled | Slovakia: 15 |

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | Ukraine: 77 |
| Country: Number of subjects enrolled | United States: 51 |
| Worldwide total number of subjects | 279 |
| EEA total number of subjects | 86 |

Notes:

| **Subjects enrolled per age group** | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 1 |
| Adults (18-64 years) | 258 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 205 sites between 5 December 2017 (first subject first visit) and 06 October 2020 (last subject last visit).

### Pre-assignment

Screening details:

A total of 279 subjects were enrolled and randomized in this study.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

Subjects received placebo matched to ontamalimab subcutaneous (SC) injection, using a prefilled syringe (PFS) on Week 0, Week 4, and Week 8 in a 12-week treatment period.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received placebo matched to ontamalimab SC injection, using a PFS.

| | |
|---|---|
| **Arm title** | Ontamalimab 25 mg |

Arm description:

Subjects received 25 milligrams (mg) of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ontamalimab |
| Investigational medicinal product code | SHP647 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 25 mg of ontamalimab SC injection, using a PFS.

| | |
|---|---|
| **Arm title** | Ontamalimab 75 mg |

Arm description:

Subjects received 75 mg of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Ontamalimab |
| Investigational medicinal product code | SHP647 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 75 mg of ontamalimab SC injection, using a PFS.

| **Number of subjects in period 1** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|---|---|---|---|
| Started | 56 | 111 | 112 |
| Completed | 49 | 103 | 105 |
| Not completed | 7 | 8 | 7 |
| Consent withdrawn by subject | 2 | 1 | 3 |
| Adverse event, non-fatal | 5 | 4 | 1 |
| Protocol Deviation | - | 3 | - |
| Pregnancy | - | - | 1 |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | - | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo matched to ontamalimab subcutaneous (SC) injection, using a prefilled syringe (PFS) on Week 0, Week 4, and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 25 mg |
| Reporting group description: | |
| Subjects received 25 milligrams (mg) of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 75 mg |
| Reporting group description: | |
| Subjects received 75 mg of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |

| Reporting group values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|---|---|---|---|
| Number of subjects | 56 | 111 | 112 |
| Age categorical<br>Units: | | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 41.6 | 43.5 | 43.9 |
| standard deviation | ± 13.50 | ± 14.16 | ± 13.08 |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 23 | 46 | 45 |
| Male | 33 | 65 | 67 |
| Race, Customized<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 5 | 3 |
| Asian: Japanese | 6 | 5 | 6 |
| Asian: Korean | 4 | 5 | 8 |
| Asian: Other | 1 | 0 | 0 |
| Black or African American | 2 | 4 | 1 |
| White | 41 | 85 | 88 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 0 |
| Multiple | 1 | 5 | 1 |
| Other (Unspecified) | 1 | 1 | 5 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 5 | 17 | 16 |
| Not Hispanic or Latino | 51 | 93 | 96 |
| Unknown or Not Reported | 0 | 1 | 0 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 279 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: | | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 114 | | |
| Male | 165 | | |
| Race, Customized<br>Units: Subjects | | | |
| American Indian or Alaska Native | 8 | | |
| Asian: Japanese | 17 | | |
| Asian: Korean | 17 | | |
| Asian: Other | 1 | | |
| Black or African American | 7 | | |
| White | 214 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |
| Multiple | 7 | | |
| Other (Unspecified) | 7 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 38 | | |
| Not Hispanic or Latino | 240 | | |
| Unknown or Not Reported | 1 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo matched to ontamalimab subcutaneous (SC) injection, using a prefilled syringe (PFS) on Week 0, Week 4, and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 25 mg |
| Reporting group description: | |
| Subjects received 25 milligrams (mg) of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 75 mg |
| Reporting group description: | |
| Subjects received 75 mg of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |

### Primary: Number of Subjects With Remission Based on Composite Score at Week 12

| | |
|---|---|
| End point title | Number of Subjects With Remission Based on Composite Score at Week 12 |
| End point description: | |
| Remission was defined as a composite score of patient-reported symptoms using daily e-diary and centrally read endoscopy as stool frequency sub-score of 0 or 1 with at least a 1-point change from baseline, rectal bleeding sub-score of 0 and endoscopic sub-score of 0 or 1 (modified, excluded friability). The composite score was a recommended measure derived from the Mayo score without the physician global assessment (PGA) sub-score and ranged from 0 to 9 points. The Mayo score was a measure of Ulcerative Colitis (UC) disease activity. It ranged from 0 to 12 points and consisted of 4 sub-scores, each graded from 0 to 3 with higher scores indicating more severe disease. The sub-scores were stool frequency (0-3); rectal bleeding (0-3); findings of endoscopy (0-3); physician global assessment (0-3). Full analysis set (FAS) consisted of all subjects in the randomized set who had received at least 1 dose of investigational product (IP). | |
| End point type | Primary |
| End point timeframe: | |
| At Week 12 | |

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 7 | 30 | 33 | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical analysis 1 |
| Comparison groups | Placebo v Ontamalimab 25 mg |

| | |
|---|---|
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.027 [1] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[1] - P-value was based on Cochran-Mantel- Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 75 mg |
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.014 [2] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[2] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

## Secondary: Number of Subjects With Endoscopic Remission at Week 12

| End point title | Number of Subjects With Endoscopic Remission at Week 12 |
|---|---|

End point description:

Endoscopic remission was defined by centrally read endoscopic sub-score 0 or 1 (modified, excluded friability). The centrally read endoscopic sub-score of Mayo score ranged from 0 to 3 with higher scores indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 7 | 39 | 38 | |

### Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 25 mg |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 [3] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[3] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 75 mg |
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 [4] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[4] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

## Secondary: Number of Subjects With Clinical Remission at Week 12

| End point title | Number of Subjects With Clinical Remission at Week 12 |
|---|---|

End point description:

Clinical remission was defined by stool frequency sub-score of 0 or 1 with at least a 1-point change from baseline in stool frequency sub-score, and rectal bleeding sub-score of 0. The stool frequency sub-score and rectal bleeding sub-score ranged from 0 to 3 with higher scores indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 10 | 50 | 56 | |

### Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 25 mg |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 [5] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[5] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 75 mg |

| | |
|---|---|
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 [6] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[6] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

## Secondary: Number of Subjects With Clinical Response Based on Composite Score at Week 12

| | |
|---|---|
| End point title | Number of Subjects With Clinical Response Based on Composite Score at Week 12 |

End point description:

Clinical response based on composite score was defined as a decrease from baseline in the composite score of patient-reported symptoms using daily e-diary and centrally read endoscopy of at least 2 points and at least 30 percent (%), with an accompanying decrease in the sub-score for rectal bleeding greater than or equal to (>=) 1 point or a sub-score for rectal bleeding less than or equal to (<=) 1. The composite score was a recommended measure derived from the Mayo score without the PGA sub-score and ranged from 0 to 9 points. The Mayo score was a measure of UC disease activity. It ranged from 0 to 12 points and consisted of 4 sub-scores, each graded from 0 to 3 with higher scores indicating more severe disease The sub-scores were stool frequency (0-3); rectal bleeding (0-3); findings of endoscopy (0-3); PGA (0-3). FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

At Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 16 | 67 | 64 | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 75 mg |
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 [7] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[7] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 25 mg |

| | |
|---|---|
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 [8] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[8] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

## Secondary: Number of Subjects With Mucosal Healing Based on Endoscopic and Histological Assessment Using the Geboes Score Grading System at Week 12

| | |
|---|---|
| End point title | Number of Subjects With Mucosal Healing Based on Endoscopic and Histological Assessment Using the Geboes Score Grading System at Week 12 |

End point description:

Mucosal healing was defined by centrally read endoscopic sub-score 0 or 1 (modified, excluded friability) and centrally read Geboes score of <=2. The centrally read endoscopic sub-score of Mayo score ranged from 0 to 3 with higher scores indicating more severe disease. Geboes score grading system, was a validated score for evaluating histologic disease activity in UC as follows: grade 0 equal to (=) structural and architectural changes; grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher Geboes score indicating more severe disease. Number of subjects with mucosal healing based on endoscopic and histological assessment using the Geboes score grading system were reported. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

At Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 6 | 35 | 30 | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 25 mg |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 [9] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[9] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

| Statistical analysis title | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Ontamalimab 75 mg |

| | |
|---|---|
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 [10] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[10] - P-value was based on Cochran-Mantel-Haenszel chi-square test stratified by actual status of prior anti-TNF treatment and glucocorticoid at baseline.

## Secondary: Number of Subjects With Remission Based on Total Mayo Score at Week 12

| | |
|---|---|
| End point title | Number of Subjects With Remission Based on Total Mayo Score at Week 12 |

End point description:

Remission was defined as a total Mayo score of <=2 with no individual sub-score (stool frequency, rectal bleeding, endoscopy [modified, excluded friability], and PGA) exceeding 1, at the Week 12. The Total Mayo score ranged from 0 to 12 points and consisted of 4 sub-scores, each graded from 0 to 3 with higher scores indicating more severe disease: stool frequency (0-3); rectal bleeding (0-3); findings of endoscopy (0-3); PGA (0-3). FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

At Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 5 | 28 | 26 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinical Response Based on Total Mayo Score at Week 12

| | |
|---|---|
| End point title | Number of Subjects With Clinical Response Based on Total Mayo Score at Week 12 |

End point description:

Clinical response (Mayo) was defined as a decrease from baseline in the total Mayo score of at least 3 points and at least 30%, with an accompanying decrease in the sub-score for rectal bleeding >=1 point or an absolute sub-score for rectal bleeding <=1. The Total Mayo score ranged from 0 to 12 points and consisted of the following 4 sub-scores, each graded from 0 to 3 with higher scores indicating more severe disease: stool frequency (0-3); rectal bleeding (0-3); findings of endoscopy (0-3); PGA (0-3). FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

At Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 19 | 66 | 63 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Partial Mayo Score <=2 With no Individual Sub-score Greater than (>) 1 at Weeks 4, 8, and 12

| End point title | Number of Subjects With Partial Mayo Score <=2 With no Individual Sub-score Greater than (>) 1 at Weeks 4, 8, and 12 |
|---|---|

End point description:

The partial Mayo score ranged from 0 to 9 points and consisted of the following 3 sub-scores, each graded from 0 to 3 with higher scores indicating more severe disease: Stool frequency (0-3); Rectal bleeding (0-3); PGA (0-3). The partial Mayo score did not include the endoscopy sub-score. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Weeks 4, 8, and 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | | | | |
| At Week 4 | 6 | 26 | 23 | |
| At Week 8 | 12 | 53 | 41 | |
| At Week 12 | 10 | 49 | 52 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinical Remission With Stool Frequency Sub-scores of 0 or 1 and Rectal Bleeding Sub-score of 0 at Weeks 4 and 8

| End point title | Number of Subjects With Clinical Remission With Stool Frequency Sub-scores of 0 or 1 and Rectal Bleeding Sub-score of 0 at Weeks 4 and 8 |
|---|---|

End point description:

Number of subjects were reported who with stool frequency sub-scores of 0 or 1 and rectal bleeding

sub-score of 0. Clinical remission was defined as stool frequency sub-score of 0 or 1 with at least a 1-point change from baseline in stool frequency sub-score, and a rectal bleeding sub-score of 0. The stool frequency sub-score and rectal bleeding sub-score of Mayo score ranges from 0 to 3 with higher scores indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Weeks 4 and 8

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | | | | |
| At Week 4 | 4 | 28 | 22 | |
| At Week 8 | 10 | 52 | 41 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Endoscopic Remission With Sub-score of 0 at Week 12

| End point title | Number of Subjects With Endoscopic Remission With Sub-score of 0 at Week 12 |
|---|---|

End point description:

Endoscopic remission was defined by centrally read endoscopic sub-score 0 (modified, excluded friability). The centrally read endoscopic sub-score of Mayo score ranged from 0 to 3 with higher scores indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 1 | 14 | 14 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinical Remission With Both Rectal Bleeding and Stool Frequency Sub-scores of 0 at Week 4, 8, and 12

| End point title | Number of Subjects With Clinical Remission With Both Rectal Bleeding and Stool Frequency Sub-scores of 0 at Week 4, 8, and 12 |
|---|---|

End point description:

Number of subjects were reported with rectal bleeding and stool frequency sub-scores of 0. Clinical remission was defined as both rectal bleeding and stool frequency sub-scores of 0. The stool frequency sub-score and rectal bleeding sub-score of Mayo score ranges from 0 to 3 with higher scores indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 4, 8, and 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | | | | |
| At Week 4 | 0 | 15 | 12 | |
| At Week 8 | 5 | 29 | 19 | |
| At Week 12 | 6 | 36 | 26 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Deep Remission at Week 12

| End point title | Number of Subjects With Deep Remission at Week 12 |
|---|---|

End point description:

Deep remission was defined as both endoscopic and rectal bleeding sub-scores of 0, and stool frequency sub-score <=1 and a centrally read Geboes score of <=2. The stool frequency sub-score, rectal bleeding sub-score and endoscopic sub-score of Mayo score ranged from 0 to 3 with higher scores indicating more severe disease. The composite score was a recommended measure consisted of the Mayo score without the PGA sub-score and ranged from 0 to 9 points. Geboes score grading system was a validated score for evaluating histologic disease activity in UC as follows: grade 0 = structural and architectural changes; grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher Geboes score indicating more severe disease. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | 1 | 11 | 9 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Average Worst Abdominal Pain Score Based on Patient Reported Outcome-ulcerative Colitis (PRO-UC) Daily e-Diary at Week 12

| End point title | Change From Baseline in Average Worst Abdominal Pain Score Based on Patient Reported Outcome-ulcerative Colitis (PRO-UC) Daily e-Diary at Week 12 |
|---|---|

End point description:

PRO-UC signs and symptom data were collected using a daily e-diary during treatment period. Collection of daily e-diary data was begun at least 10 days before the baseline visit. Subjects asked to record data of abdominal pain worst severity, over previous 24 hours, in the e-diary. Subjects signs and symptom average scores at each scheduled visit were calculated based on data recorded over most recent 3 days (consecutive or non-consecutive) of last 10 days prior to scheduled visit start date excluding following days: day of any bowel preparation, day of endoscopy, any days between day of bowel preparation and day of endoscopy and 2 days after day of endoscopy. Abdominal pain's worst severity assessment was based on 11-point numerical rating scale with 0-No pain and 10-Worst imaginable pain over the previous 24 hours. Higher scores indicating more severe pain. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | -1.69 (± 0.309) | -2.49 (± 0.218) | -1.83 (± 0.215) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Diarrhea (Average Loose Bowel Movements) Score Based on PRO-UC Daily e-Diary at Week 12

| End point title | Change From Baseline in Diarrhea (Average Loose Bowel Movements) Score Based on PRO-UC Daily e-Diary at Week 12 |
|---|---|

End point description:

PRO-UC signs and symptom data were collected using a daily e-diary during treatment period. Collection of daily e-diary data was begun at least 10 days before the baseline visit. Subjects were asked to record

the signs and symptom data for number of loose bowel movement, as experienced over the previous 24 hours, in the e-diary. Subjects signs and symptom average scores at each scheduled visit were calculated based on data recorded over the most recent 3 days (consecutive or nonconsecutive) of the last 10 days prior to the scheduled visit start date excluding the following days: day of any bowel preparation, day of endoscopy, any days between day of bowel preparation and day of endoscopy, and the 2 days after the day of endoscopy. Average number of loose bowel movement ranged from 0-27. Higher scores indicating more frequent bowel movements. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | -1.41 (± 0.405) | -3.50 (± 0.286) | -2.87 (± 0.284) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Average Bowel Movements With Urgency Score Based on PRO-UC Daily e-Diary at Week 12 at Week 12

| End point title | Change From Baseline in Average Bowel Movements With Urgency Score Based on PRO-UC Daily e-Diary at Week 12 at Week 12 |
|---|---|

End point description:

PRO-UC signs and symptom data were collected using a daily e-diary during treatment period. Collection of daily e-diary data was begun at least 10 days before the baseline visit. Subjects were asked to record the signs and symptom data for number of bowel movement with urgency, as experienced over the previous 24 hours. Subjects signs and symptom average scores at each scheduled visit were calculated based on data recorded over the most recent 3 days (consecutive or nonconsecutive) of the last 10 days prior to the scheduled visit start date excluding the following days: day of any bowel preparation, day of endoscopy, any days between day of bowel preparation and day of endoscopy, and the 2 days after the day of endoscopy. Average number bowel movements urgency ranged from 0-27. Higher scores indicating more frequent bowel movements. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | -1.09 (± 0.373) | -2.87 (± 0.263) | -2.56 (± 0.264) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Absolute Stool Frequency (Average Number of Bowel Movements) Score Based on PRO-UC Daily e-Diary at Week 12

| End point title | Change From Baseline in Absolute Stool Frequency (Average Number of Bowel Movements) Score Based on PRO-UC Daily e-Diary at Week 12 |
|---|---|

End point description:

PRO-UC signs and symptom data were collected using a daily e-diary during treatment period. Collection of daily e-diary data was begun at least 10 days before the baseline visit. Subjects were asked to record the signs and symptom data for average number of bowel movements, as experienced over the previous 24 hours. Subjects signs and symptom average scores at each scheduled visit were calculated based on data recorded over the most recent 3 days (consecutive or nonconsecutive) of the last 10 days prior to the scheduled visit start date excluding the following days: day of any bowel preparation, day of endoscopy, any days between day of bowel preparation and day of endoscopy, and the 2 days after the day of endoscopy. Average number bowel movements ranged from 0-27. Higher scores indicating more frequent bowel movements. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | -1.26 (± 0.386) | -3.32 (± 0.272) | -2.97 (± 0.272) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Absolute Rectal Bleeding (Average Number Bowel Movements With Blood) Score Based on PRO-UC Daily e-Diary at Week 12

| End point title | Change From Baseline in Absolute Rectal Bleeding (Average Number Bowel Movements With Blood) Score Based on PRO-UC Daily e-Diary at Week 12 |
|---|---|

End point description:

PRO-UC signs and symptom data were collected using a daily e-diary during treatment period. Collection of daily e-diary data was begun at least 10 days before the baseline visit. Subjects asked to record data for average number of bowel movements with blood, as experienced over the previous 24 hours. Subjects signs and symptom average scores at each scheduled visit were calculated based on data recorded over the most recent 3 days (consecutive or nonconsecutive) of the last 10 days prior to the scheduled visit start date excluding the following days: day of any bowel preparation, day of endoscopy, any days between day of bowel preparation and day of endoscopy, and the 2 days after the day of endoscopy. Average number bowel movements with blood ranged from 0 to 27. Higher scores indicating more frequent bowel movements with blood. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | -2.05 (± 0.379) | -3.74 (± 0.267) | -3.41 (± 0.265) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline in Total Sign/Symptom Score Based on PRO-UC Daily e-Diary at Week 12**

| End point title | Change From Baseline in Total Sign/Symptom Score Based on PRO-UC Daily e-Diary at Week 12 |
|---|---|

End point description:

Total sign/symptom score was the average of the average scores of worst abdominal pain over the past 24 hours and the conversion scale values for number of bowel movements blood, number of bowel movements with urgency, number of bowel movements and number of loose bowel movements, with scale ranged of 0-10, with higher scores indicating higher severity. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 104 | 107 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | -1.15 (± 0.246) | -2.32 (± 0.173) | -2.00 (± 0.172) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Domains Scores at Weeks 8 and 12

| End point title | Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Domains Scores at Weeks 8 and 12 |
|---|---|

End point description:

IBDQ was a psychometrically validated PRO instrument for measuring the disease-specific health-related quality of life (HRQL) in subjects with inflammatory bowel disease, including UC. The IBDQ consisted of 32 items, which were grouped into 4 dimensions: bowel function, emotional status, systemic symptoms, and social function. The 4 domains were scored as follows: Bowel symptoms (BS): 10 to 70; Systemic symptoms (SS): 5 to 35; Emotional function (EF): 12 to 84; Social function (SF): 5 to 35. Higher scores indicating a better quality of life. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint and n=number analysed refer to subjects evaluable at specific time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 8 and 12

| **End point values** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 53 | 108 | 106 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | | | | |
| BF: Change at Week 8 (n=53, 108, 106) | 9.59 (± 1.611) | 16.66 (± 1.189) | 15.36 (± 1.180) | |
| BF: Change at Week 12 (n=50, 104, 106) | 9.51 (± 1.707) | 17.71 (± 1.250) | 15.86 (± 1.232) | |
| ES: Change at Week 8(n=53, 108, 106) | 8.91 (± 1.701) | 15.18 (± 1.255) | 14.41 (± 1.247) | |
| ES: Change at Week 12(n=50, 104, 106) | 9.94 (± 1.861) | 14.84 (± 1.359) | 14.73 (± 1.341) | |
| SS: Change at Week 8 (n=53, 108, 106) | 3.84 (± 0.759) | 6.61 (± 0.561) | 5.86 (± 0.557) | |
| SS: Change at Week 12(n=50, 104, 106) | 3.85 (± 0.814) | 7.34 (± 0.596) | 6.04 (± 0.587) | |
| SF: Change at Week 8(n=53, 108, 106) | 5.06 (± 0.873) | 6.97 (± 0.643) | 6.75 (± 0.640) | |
| SF: Change at Week 12 (n=50, 104, 106) | 5.09 (± 0.926) | 7.68 (± 0.677) | 7.03 (± 0.668) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Total Scores in IBDQ at Weeks 8 and 12

| End point title | Change From Baseline in Total Scores in IBDQ at Weeks 8 and 12 |
|---|---|

End point description:

IBDQ was a psychometrically validated PRO instrument for measuring the disease-specific HRQL in subjects with inflammatory bowel disease, included UC. The IBDQ consisted of 32 items, which were grouped into 4 dimensions: bowel function, emotional status, systemic symptoms, and social function. The 4 domains were scored as follows: Bowel symptoms: 10 to 70; Systemic symptoms: 5 to 35; Emotional function: 12 to 84; Social function: 5 to 35. The total IBDQ score ranged from 32 to 224. For the total score and each domain, a higher score indicating better HRQL. A score of at least 170 corresponds to clinical remission and an increase of at least 16 points was considered to indicate a clinically meaningful improvement. FAS: all subjects in the randomized set who had received at least 1 dose of IP. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint and n=number analysed refer to subjects evaluable at specific time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 8 and 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 53 | 108 | 106 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 8 (n=53, 108, 106) | 27.56 (± 4.574) | 45.63 (± 3.380) | 42.58 (± 3.358) | |
| Change at Week 12 (n=50, 104, 106) | 28.39 (± 4.990) | 47.75 (± 3.649) | 43.85 (± 3.604) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Short Form-36 Health Survey (SF-36), Version 2, Acute (Physical and Mental Component Summary Scores) at Week 12

| End point title | Change From Baseline in Short Form-36 Health Survey (SF-36), Version 2, Acute (Physical and Mental Component Summary Scores) at Week 12 |
|---|---|

End point description:

SF-36 was a generic quality-of-life instrument that had been widely used to assess HRQL of subjects. SF-36 consisted of 36 items that were aggregated into 8 multi-item scales (physical functioning [1=yes, limited a lot to 3=no, not limited at all], role-physical [1=all of the time to 5=none of the time], bodily pain [1=very severe to 6=none], general health [1=poor to 5=excellent], vitality [1=none of the time to 5=all of the time], social functioning [1=all of the time: to 5=none of the time], role emotional [1=all of the time to 5=none of the time] and mental health [1=all of the time to 5=none of the time]). Four domains; PCS score (physical functioning, role-physical, bodily pain, general health) and MCS score (vitality, social functioning, role-emotional, mental health). Scores ranged from 0 to 100.Higher scores indicating better HRQL. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 104 | 106 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | | | | |
| Mental Component: Change at Week 12 | 2.09 (± 1.301) | 7.37 (± 0.949) | 6.68 (± 0.935) | |
| Physical Component: Change at Week 12 | 4.84 (± 0.982) | 6.45 (± 0.721) | 5.54 (± 0.709) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Short Form-36 Health Survey (SF-36), Version 2, Acute (Individual Domain Scores) at Week 12

| End point title | Change From Baseline in Short Form-36 Health Survey (SF-36), Version 2, Acute (Individual Domain Scores) at Week 12 |
|---|---|

End point description:

SF-36 was a generic quality-of-life instrument that had been widely used to assess HRQL of subjects. Generic instruments were used in general populations to assess a wide range of domains applicable to a variety of health states, conditions, and diseases. SF-36 consisted of 36 items that were aggregated into 8 multi-item scales (physical functioning [1=yes, limited a lot to 3=no, not limited at all], role-physical [1=all of the time to 5=none of the time], bodily pain [1=very severe to 6=none], general health [1=poor to 5=excellent], vitality [1=none of the time to 5=all of the time], social functioning [1=all of the time: to 5=none of the time], role emotional [1=all of the time to 5=none of the time] and mental health [1=all of the time to 5=none of the time]), with scores ranged from 0 to 100. Higher scores indicating better HRQL. Analysis was performed using FAS. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 104 | 106 | |
| Units: Score on a Scale | | | | |
| least squares mean (standard error) | | | | |
| Physical Functioning: Change at Week 12 | 3.40 (± 0.901) | 5.03 (± 0.657) | 3.79 (± 0.646) | |
| Role-Physical: Change at Week 12 | 4.47 (± 1.205) | 7.39 (± 0.884) | 6.90 (± 0.874) | |
| Bodily Pain: Change at Week 12 | 5.55 (± 1.293) | 8.18 (± 0.941) | 7.06 (± 0.926) | |
| General Health: Change at Week 12 | 3.93 (± 1.203) | 7.00 (± 0.880) | 6.34 (± 0.865) | |
| Vitality: Change at Week 12 | 3.59 (± 1.381) | 8.23 (± 1.008) | 7.43 (± 0.993) | |

| | | | | |
|---|---|---|---|---|
| Social Functioning: Change at Week 12 | 3.59 (± 1.233) | 7.43 (± 0.898) | 6.54 (± 0.884) | |
| Role-Emotional: Change at Week 12 | 1.27 (± 1.317) | 5.79 (± 0.958) | 5.68 (± 0.944) | |
| Mental Health: Change at Week 12 | 3.56 (± 1.268) | 7.90 (± 0.925) | 6.47 (± 0.911) | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Based on Inpatient Hospitalization

| End point title | Number of Subjects Based on Inpatient Hospitalization |
|---|---|

End point description:

Number of subjects based on inpatient hospitalization due to all-cause hospitalization, gastrointestinal related, Other illness/problem, and undergo gastrointestinal related procedures during the entire study period were reported. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

| End point type | Secondary |
|---|---|

End point timeframe:

From start of study up to follow up (Week 29)

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 111 | 112 | |
| Units: Subjects | | | | |
| All-Cause Hospitalization | 2 | 3 | 2 | |
| Gastrointestinal Related | 1 | 2 | 1 | |
| Other Illness/Problem | 1 | 2 | 2 | |
| Undergo Gastrointestinal Related Procedures | 1 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Median Duration of Total Inpatient Days

| End point title | Median Duration of Total Inpatient Days |
|---|---|

End point description:

Inpatient days were calculated as date of discharge - date of admission + 1. Median duration of total inpatient days during the entire study period was reported. FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP. Here, number of subjects analysed signifies subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

From start of study up to follow-up (Week 29)

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2 | 3 | 2 | |
| Units: Days | | | | |
| median (full range (min-max)) | 10.5 (6 to 15) | 7.0 (6 to 11) | 2.0 (2 to 2) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From start of study drug administration up to follow-up (Week 29) | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo matched to ontamalimab subcutaneous (SC) injection, using a prefilled syringe (PFS) on Week 0, Week 4, and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 25 mg |
| Reporting group description: | |
| Subjects received 25 milligrams (mg) of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |
| Reporting group title | Ontamalimab 75 mg |
| Reporting group description: | |
| Subjects received 75 mg of ontamalimab SC injection, using a PFS on Week 0, Week 4 and Week 8 in a 12-week treatment period. | |

| Serious adverse events | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 56 (7.14%) | 5 / 111 (4.50%) | 3 / 112 (2.68%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 1 / 112 (0.89%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 111 (0.00%) | 1 / 112 (0.89%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 3 / 56 (5.36%) | 1 / 111 (0.90%) | 1 / 112 (0.89%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Hydrocalyx | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 111 (0.00%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 111 (0.90%) | 0 / 112 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 56 (12.50%) | 5 / 111 (4.50%) | 7 / 112 (6.25%) |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 56 (7.14%) | 2 / 111 (1.80%) | 7 / 112 (6.25%) |
| occurrences (all) | 5 | 2 | 9 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 4 / 56 (7.14%) | 3 / 111 (2.70%) | 2 / 112 (1.79%) |
| occurrences (all) | 5 | 3 | 3 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 September 2018 | Protocol Amendment 1:<br>- Updated exclusion criteria to further define the exclusion of subjects with colitis, a history of positive Mycobacterium tuberculosis (TB), or compromised liver function.<br>- Updated exclusion criteria to indicate exclusion of subjects with prior nonbiologic treatment with immunomodulatory properties or prior apheresis or plasma exchange within the specified timeframe.<br>- Added a new section to provide appropriate guidance on patients who have been enrolled with elevated liver function test (LFT) values or who experience an increase in LFT(s) during the study. |
| 11 November 2019 | Protocol Amendment 2:<br>- Updated text to reflect preliminary results of an ePPND toxicity study in nonhuman primates, which indicated that, at the dose levels tested (30 mg/kg and 60 mg/kg), infant losses were increased in ontamalimab-exposed animals when compared both to control animals in the study and to the historical control animal data from the testing facility. The relevance of this finding to humans was unknown but could not be excluded.<br>- Added text to address FDA recommendation to evaluate the risk of hypersensitivity reactions in the Phase 3 studies and aid in the collection of relevant safety data. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated as per the sponsor decision to discontinue the SHP647 (ontamalimab) clinical trial development program for inflammatory bowel diseases (IBD) early.

Notes: